

REMARKS

Claim Rejections Under U.S.C §103

Claims 16, 32-43 and 60 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over Burkhardt P. *et al.*, in RICE GENETICS III; Proceeding of the Third International Rice Genetics Symposium; International Rice Research Institute (IRRI), 1996; Khush G. S. ed., in view of Shewmaker C. in WO 99/07867 published 18 February 1999.

The Examiner states that “Burkhardt teaches a method of transforming rice plant...with DNA molecules capable of expressing in plant cells consisting of a phytoene synthase and phytoene desaturase from daffodil, using either the CaMV35S or the endosperm tissue specific rice *Gtl* promoter, and the *hpt* hygromycin antibiotic selection gene under control of a constitutive promoter and suggest a strategy for using single genes or combinations of genes from the carotenoid biosynthetic pathway...” The Examiner also notes that Burkhardt discloses rice plants transformed with phytoene synthase and phytoene desaturase from daffodil, but acknowledges that it does not teach a bacterial phytoene desaturase. The Examiner goes on to say that Shewmaker “teaches transformation of Brassica napus plants with *crtB* and *crtI* from *E. uredovora* fused to the pea Rubisco small subunit transit peptide; wherein the transformed plants produced seeds that had several hundred fold increase of β -carotene...and that genes for plant phytoene saturase and bacterial phytoene desaturases were known in the art.”

The Examiner concludes from the above statements that it would have been obvious to modify “Burkhardt to include the polynucleotide encoding the *Erwinia uredova* bacterial phytoene desaturase and the vector encoding system derived from *A. tumefaciens* taught by Shewmaker.”

Applicants disagree with the Examiner’s assertions. Applicants note that Burkhardt suggests (page 819) that four enzymes are necessary for β -carotene biosynthesis in the rice endosperm (phytoene synthase, phytoene desaturase, ζ -carotene desaturase and lycopene cyclase). This fact clearly teaches away from the present invention. The methods of the present invention do not require a “complete set” of carotenoid biosynthetic genes in order to produce β -carotene in the rice endosperm. Indeed, it came as a surprise that β -carotene, rather than lycopene, accumulation was achieved via the use of only a plant phytoene synthase and a bacterial phytoene desaturase (as evidenced in Ye X. *et al.* Science, 14 January 2000; Vol. 287, pp. 303-305, previously cited by the Examiner) in the absence of engineering into the

rice plant a lycopene cyclase. Thus, as stated Burkhardt can be seen to teach away from the present invention.

Burkhardt also discloses a transgenic rice plant purported to comprise a plant (daffodil) phytoene synthase and a plant (daffodil) phytoene desaturase. It is reported that the transgenic rice plant accumulated a single carotenoid (phytoene) but not ζ -carotene, the product of phytoene desaturase (page 820). Burkhardt, however, still does not solve the problem of the production of carotenoids other than phytoene in the rice endosperm – since the phytoene desaturase that was introduced did not result in the accumulation of ζ -carotene as expected.

Furthermore, contrary to the Examiner's assertion in the instant Office Action, Burkhardt does not teach, or even suggest, a method by which β -carotene can be produced in the rice endosperm. By stating that the four enzymes are necessary for β -carotene biosynthesis in rice endosperm, Burkhardt has not suggested a method for producing β -carotene, they have only stated what was at that time the prevailing view in the art. Such a statement can not be viewed as a suggestion or teaching of a method for producing β -carotene biosynthesis in rice endosperm. Even if this were a proposed method, the four enzymes mentioned in Burkhardt are not required by the instant invention and thus teach away from instant invention. The inventors specifically used a bacterial desaturase to get around the need for four separate enzymes. (Ye at 303)

In any event, there is certainly no teaching or suggestion in Burkhardt that β -carotene can be produced in the rice endosperm by replacing the plant phytoene desaturase with a bacterial phytoene desaturase. The sole contribution to the obviousness determination provided by Burkhardt is the use of plant phytoene saturase, in combination with other plant enzymes to attempt biosynthesis of β -carotene in rice endosperm.

The Examiner relies on Shewmaker to provide the necessary suggestion to replace plant phytoene desaturase with a bacterial phytoene desaturase. While it is true that Shewmaker discloses the use of bacterial phytoene desaturase in Brassica napus in an attempt to **increase** β -carotene biosynthesis in Brassica napus, there are several factors that make it unlikely that it would be obvious to one of ordinary skill in the art to modify the teachings of Burkhardt with those of Shewmaker. For one, Shewmaker uses bacterial phytoene desaturase in combination with other bacterial enzymes. Shewmaker makes reference to the availability of both plant and bacterial enzymes, however, never mentions that the two can be used in combination. The omission of any reference to such a combination in a document that cites

the known availability of both suggests that the combination was not obvious, not that it would be an obvious and desirable alteration as the Examiner's rejection infers.

Also, Shewmaker is focusing on *Brassica napus* and not on rice endosperm. Not only is this an entirely different plant, as well as a different type of plant (grain v. vegetable), *Brassica napus* **already produces** β -carotene. Shewmaker's approach was to transform plants that already produced β -carotene by introducing bacterial phytoene synthase and bacterial phytoene desaturase. Thus, Shewmaker provides no information about whether these bacterial enzymes would be successful in bringing about β -carotene biosynthesis in a plant that did not already possess the inherent capability to produce β -carotene. Moreover, without this information, it clearly could not have been obvious to one of the ordinary skill in the art to modify the β -carotene introducing method of Burkhardt with the β -carotene increasing method of Shewmaker as there would be no expectation that the bacterial enzymes would even work in rice endosperm, a non- β -carotene producing plant, let alone whether the bacterial phytoene desaturase would work in tandem with a plant phytoene saturase. This is further supported by the evidence that in Burkhardt the transformation of rice endosperm with plant enzymes did not even yield the desired and expected result, that is, the accumulation of β -carotene.

Neither Burkhardt or Shewmaker specifically disclose a method comprising a combination of a plant phytoene synthase and a bacterial phytoene desaturase. Nor do these references disclose such a method when viewed together. The Examiner has stated that it would be obvious to combine separate and distinct elements disclosed in the two references in order to arrive at the present invention, however, this is simply not the case. There is no suggestion in either Burkhardt or Shewmaker that β -carotene accumulation could be achieved in the rice endosperm by the use of a plant phytoene synthase and a bacterial phytoene desaturase (e.g. *crt I*) alone. Although it is *possible* to combine the disclosures of Burkhardt and Shewmaker and arrive at the present invention, there is absolutely no motivation or any reason to conclude that one of ordinary skill in the art would do so in the absence of the present invention. In doing so, it is submitted that the Examiner has made an *ex-post facto* analysis, improperly based on hindsight, and has also improperly gone outside the prior art, and the knowledge possessed by one of ordinary skill in the art to find the necessary motivation. Thus, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants respectfully request reconsideration of the claims on the merits in light of the foregoing remarks, and allowance of the pending claims. Should the Examiner consider a telephone call to the attorney for Applicants to be helpful in progressing the case to allowance one is earnestly requested.

Respectfully submitted,



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Melissa Hardy

Name



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